

Listing of Claims.

Please amend the claims as shown below by deleting the material indicated by strike-through and adding the underlined material. This listing of claims will replace all prior versions and listings of the claims in this application.

1. (Previously presented) A propagation-defective adenovirus vector comprising a recombinant adenovirus genome that lacks a coding sequence for a functional 100K protein.
2. (Previously presented) The adenovirus of Claim 1, wherein said adenovirus can be propagated in a transcomplementing cell.
3. (Original) The adenovirus of Claim 1, wherein said adenovirus can be propagated in a transcomplementing cell in the absence of a helper.
4. (Previously presented) The adenovirus of Claim 1, wherein said adenovirus genome further lacks an E1 region or comprises an E1 region comprising one or more deletion(s) therein.
5. (Previously presented) The adenovirus of Claim 1, wherein said adenovirus genome further lacks an E3 region or comprises an E3 region comprising one or more deletion(s) therein.

Claims 6-12. (Canceled)

13. (Previously presented) The adenovirus of Claim 1, wherein said adenovirus genome comprises a 100K region comprising a deletion at about nucleotides 24,990 to 25,687 of the adenovirus serotype 5 genome or a corresponding region of the genome of adenoviruses of other serotypes.

- 14. (Canceled)
- 15. (Previously presented) The adenovirus of Claim 4, wherein said adenovirus is disclosed herein as [E1⁺, 100K⁻]Ad.
- 16. (Original) The adenovirus of Claim 15, wherein said adenovirus comprises one or more heterologous nucleotide sequences.

Claims 17 -24. (Canceled)

- 25. (Original) The adenovirus of Claim 1 further comprising one or more heterologous nucleotide sequences.
- 26. (Original) The adenovirus of Claim 25, wherein said heterologous nucleotide sequence(s) is operatively associated with expression control sequences.
- 27. (Original) The adenovirus of Claim 26, wherein said expression control sequences include a promoter.
- 28. (Original) The adenovirus of Claim 27, wherein said promoter is selected from the group consisting of liver-specific, muscle-specific, and brain-specific promoters.
- 29. (Original) The adenovirus of Claim 27, wherein said promoter is selected from the group consisting of the CMV promoter, albumin promoter, EF1- α promoter, PyK promoter, MFG promoter, and Rous sarcoma virus promoter.

30. (Previously presented) The adenovirus of Claim 25, wherein said adenovirus genome further comprises an adenovirus E1A enhancer sequence.
31. (Original) The adenovirus of Claim 25, wherein said heterologous nucleotide sequence(s) encodes a protein or peptide.
32. (Original) The adenovirus of Claim 31, wherein said protein or peptide is a therapeutic protein or peptide.
33. (Original) The adenovirus of Claim 31, wherein said protein or peptide is an immunogenic protein or peptide.
34. (Original) The adenovirus of Claim 31, wherein said protein or peptide is a reporter protein or peptide.
35. (Currently amended) The adenovirus of Claim 25 ~~34~~, wherein said heterologous nucleotide sequence(s) encodes an antisense nucleotide sequence or non-translated RNA.
36. (Original) The adenovirus of Claim 31, wherein said protein or peptide is a lysosomal protein.
37. (Original) The adenovirus of Claim 31, wherein said protein or peptide is associated with a metabolic disorder.
38. (Original) The adenovirus of Claim 37, wherein said protein or peptide is associated with a lysosomal storage disease.

39. (Original) The adenovirus of Claim 38, wherein said protein or peptide is selected from the group consisting of β -galactosidase, β -hexosaminidase A, β -hexosaminidase B, GM₂ activator protein, glucocerebrosidase, arylsulfatase A, galactosylceramidase, acid sphingomyelinase, acid ceramidase, acid lipase, α -L-iduronidase, iduronate sulfatase, heparan N-sulfatase, α -N-acetylglucosaminidase acetyl-CoA, glucosaminide acetyltransferase, N-acetylglucosamine-6-sulfatase, arylsulfatase B, β -glucuronidase, α -mannosidase, β -mannosidase, α -L-fucosidase, N-aspartyl- β -glucosaminidase, α -neuraminidase, lysosomal protective protein, α -N-acetyl-galactosaminidase, N-acetylglucosamine-1-phosphotransferase, cystine transport protein, sialic acid transport protein, the CLN3 gene product, palmitoyl-protein thioesterase, saposin A, saposin B, saposin C, and saposin D.
40. (Original) The adenovirus of Claim 37, wherein said protein or peptide is associated with a glycogen storage disease.
41. (Original) The adenovirus of Claim 40, wherein said protein or peptide is selected from the group consisting of glucose 6-phosphatase, lysosomal acid α glucosidase, glycogen debranching enzyme, branching enzyme, muscle phosphorylase, liver phosphorylase, phosphorylase kinase, muscle phosphofructokinase, glycogen synthase, phosphoglucoisomerase, muscle phosphoglycerate kinase, phosphoglycerate mutase, and lactate dehydrogenase.

Claims 42-58. (Canceled)

59. (Previously presented) A propagation-defective adenovirus vector comprising a recombinant adenovirus genome that lacks a functional coding sequence for

a 100K protein and comprises a heterologous nucleotide sequence encoding a lysosomal acid α -glucosidase.

60. (Previously presented) The adenovirus of Claim 59, wherein said adenovirus genome comprises a polymerase region comprising a deletion at about nucleotides 7274 to 7881 of the adenovirus serotype 5 genome or a corresponding region of the genome of adenoviruses of other serotypes.
61. (Previously presented) The adenovirus of Claim 59, wherein said adenovirus comprises a preterminal protein region comprising a deletion at about nucleotides 9198 to 9630 of the adenovirus serotype 5 genome or a corresponding region of the genome of adenoviruses of other serotypes.
62. (Previously presented) The adenovirus of Claim 59, wherein said adenovirus genome (a) lacks a polymerase region or comprises a polymerase region comprising one or more deletions therein and (b) lacks a preterminal protein region or comprises a preterminal protein region comprising one or more deletions therein.
63. (Original) The adenovirus of Claim 59, wherein said heterologous nucleotide sequence is operatively associated with a promoter.
64. (Original) The adenovirus of Claim 63, wherein said promoter is selected from the group consisting of liver-specific and muscle-specific promoters.
65. (Original) The adenovirus of Claim 63, wherein said promoter is selected from the group consisting of the CMV promoter, albumin promoter, EF1- α promoter, PyK promoter, MFG promoter, and Rous sarcoma virus promoter.

- 66. (Previously presented) The adenovirus of Claim 59, wherein said protein or peptide is human lysosomal acid α -glucosidase.
- 67. (Previously presented) The adenovirus of Claim 59, wherein said adenovirus genome comprises a 100K region comprising a deletion at about nucleotides 24,990 to 25,687 of the adenovirus serotype 5 genome or a corresponding region of the genome of adenoviruses of other serotypes.
- 68. (Previously presented) The adenovirus of Claim 59, wherein said adenovirus genome comprises a IVa2 region comprising a deletion at about nucleotides 4830 to 5766 of the adenovirus serotype 5 genome or a corresponding region of adenoviruses of other serotypes.
- 69. (Previously presented) A mammalian cell comprising the adenovirus of Claim 1.
- 70. (Original) The cell of Claim 69, wherein said adenovirus comprises one or more heterologous nucleotide sequences encoding a protein or peptide.

Claims 71-74. (Canceled)

- 75. (Previously presented) A mammalian cell comprising the adenovirus of Claim 59.

Claims 76-79. (Canceled)

- 80. (Currently amended) An isolated mammalian cell comprising an isolated DNA comprising a nucleotide sequence encoding an adenovirus 100K protein, wherein said isolated DNA is stably integrated into the genome of said cell,

and wherein said cell can propagate an adenovirus genome that essentially lacks expression of a functional 100K protein.

- 81. (Canceled)
- 82. (Currently amended) The cell of Claim 80 ~~84~~, wherein said cell is a K-16 cell.
- 83. (Previously presented) The cell of Claim 80, wherein said nucleotide sequence further encodes a constitutive promoter that is operatively associated with the sequence encoding said adenovirus 100K protein.
- 84. (Original) The cell of Claim 83, wherein said cell is a C7 cell constitutively expressing the 100K protein.
- 85. (Previously presented) The cell of Claim 80, wherein said nucleotide sequence encodes an inducible promoter that is operatively associated with the sequence encoding said adenovirus 100K protein.
- 86. (Previously presented) The cell of Claim 80, further comprising a recombinant adenovirus genome, wherein said adenovirus genome lacks a coding sequence for a functional 100K protein.

Claims 87-93. (Canceled)

- 94. (Previously presented) An isolated DNA comprising a recombinant adenovirus genome that lacks a coding sequence for a functional 100K protein.

95. (Previously presented) The isolated DNA of Claim 94, wherein said adenovirus genome comprises a 100K region comprising a deletion at about nucleotides 24,990 to 25,687 of the adenovirus serotype 5 genome or a corresponding region of the genome of adenoviruses of other serotypes.
96. (Original) A vector comprising the isolated DNA of Claim 94.
97. (Original) The vector of Claim 96, wherein said vector is a plasmid.
98. (Original) The vector of Claim 97, wherein said vector is disclosed herein as pcDNA3+100K.

Claims 99-104 (Canceled)

105. (Previously presented) A method of producing a propagation-defective adenovirus vector, comprising:
- introducing a propagation-defective adenovirus into a mammalian cell, wherein the introduced adenovirus comprises a recombinant adenovirus genome that lacks a coding sequence for a functional 100K protein;
 - wherein the mammalian cell expresses a functional 100K protein and transcomplements the function(s) lacking from the adenovirus genome; and
 - collecting the propagation-defective adenovirus vector.
106. (Original) The method of Claim 105, wherein the collected adenovirus has a titer of at least 100 infectious units per cell.

107. (Currently amended) The method of Claim 105, wherein the adenovirus genome further lacks an ~~and~~ E1 region or comprises an E1 region comprising one or more deletion(s) therein.
108. (Previously presented) The method of Claim 105, wherein the adenovirus genome further lacks an E3 region or comprises an E3 region comprising one or more deletion(s) therein.
109. (Previously presented) The method of Claim 105, wherein the adenovirus genome further lacks a polymerase region or comprises a polymerase region comprising one or more deletion(s) therein.
110. (Canceled)
111. (Previously presented) The method of Claim 105, wherein the adenovirus genome comprises a 100K region comprising a deletion at about nucleotides 24,990 to 25,687 of the adenovirus serotype 5 genome or a corresponding region of the genome of adenoviruses of other serotypes.
112. (Previously presented) The method of Claim 111, wherein the adenovirus is disclosed herein as [E1⁻, 100K]Ad.
113. (Previously presented) The method of Claim 105, wherein the mammalian cell comprises a nucleotide sequence encoding a functional 100K protein stably integrated into the genome of the mammalian cell.
114. (Original) The method of Claim 113, wherein the mammalian cell is a K-16 cell.

115. (Previously presented) The method of Claim 113, wherein the mammalian cell constitutively expresses the functional 100K protein.
116. (Original) The method of Claim 115, wherein the mammalian cell is a C7 cell constitutively expressing the 100K protein.

Claims 117-131 (Canceled)

132. (Original) The method of Claim 105, wherein the adenovirus genome further comprises one or more heterologous nucleotide sequences.
133. (Previously presented) A composition comprising a plurality of the propagation-defective adenovirus vector produced by the method of Claim 105.

Claims 134-145 (Canceled)

146. (Previously presented) A method of producing a propagation-defective adenovirus vector, comprising:
- introducing a bacterial plasmid comprising a recombinant adenovirus genome into a bacterial cell, wherein said adenovirus genome lacks a coding sequence for a functional 100K protein;
 - amplifying the bacterial plasmid in the bacterial cell;
 - recovering the amplified bacterial plasmid from the bacterial cell;
 - linearizing the recovered bacterial plasmid;
 - introducing the linearized plasmid into a mammalian cell that transcomplements the deleted functions in the adenovirus genome; and
 - collecting the propagation-defective adenovirus vector.

147. (Original) The method of Claim 146, wherein the adenovirus genome further comprises one or more heterologous nucleotide sequences.
148. (Original) The method of Claim 147, wherein the heterologous nucleotide sequence(s) encodes a lysosomal acid α -glucosidase.

Claims 149-206 (Canceled)

207. (Previously presented) A method of producing a gutted adenovirus containing a minichromosome, comprising:
introducing into a mammalian cell expressing a functional 100K protein:
 a plasmid comprising an adenovirus inverted terminal repeat (ITR), an adenovirus packaging sequence, and a heterologous nucleotide sequence, and
 a helper adenovirus comprising a recombinant adenovirus genome that lacks a coding sequence for a functional 100K protein;
collecting the gutted adenovirus containing the minichromosome from the mammalian cell.
208. (Previously presented) The method of Claim 207, wherein the adenovirus genome comprises a 100K region comprising a deletion at about nucleotides 24,990 to 25,687 of the adenovirus serotype 5 genome or a homologous region adenoviruses of other serotypes.
209. (Previously presented) The method of Claim 207, wherein the helper adenovirus is disclosed herein as [E1⁻, 100K]Ad.

210. (Previously presented) The method of Claim 207, wherein the adenovirus genome further lacks a coding sequence for a functional IVa2 protein and the mammalian cell expresses a functional IVa2 protein.
211. (Previously presented) The method of Claim 207, wherein the adenovirus genome further lacks a coding sequence for a functional polymerase protein and the mammalian cell expresses a functional polymerase protein.
212. (Previously presented) The method of Claim 207, wherein the adenovirus genome further lacks a coding sequence for a functional preterminal protein and the mammalian cell expresses a functional preterminal protein.
213. (Original) The method of Claim 207, wherein the nucleotide sequence encoding the functional 100K protein is stably integrated into the genome of the mammalian cell.
214. (Original) The method of Claim 213, wherein the mammalian cell is a K-16 cell.
215. (Original) The method of Claim 207, wherein the mammalian cell constitutively expresses the functional 100K protein.
216. (Original) The method of Claim 215, wherein said mammalian cell is a C7 cell constitutively expressing the 100K protein.
217. (Original) The method of Claim 207, wherein the helper adenovirus lacks a packaging sequence.

- 218. (Original) The method of Claim 207, wherein the helper adenovirus has a modified packaging signal that does not promote the encapsidation of the helper plasmid.
- 219. (Previously presented) The method of Claim 207, wherein the helper adenovirus further comprises lox sites flanking the packaging sequence and the mammalian cell produces the cre recombinase protein.
- 220. (Original) A method of delivering a nucleotide sequence into a cell comprising introducing into the cell a composition comprising a plurality of the gutted adenovirus particles of Claim 207.
- 221. (Original) The method of Claim 220, wherein said introducing is carried out *in vivo*.
- 222. (Original) The method of Claim 207, further comprising the step of separating the gutted adenovirus from contaminating helper adenovirus.

Claims 223-236 (Canceled)